III. REMARKS

Claim Status

Claims 10, 14-24, 41-46 are pending. Claims 41-42 are 44-46 have been considered on the merits to the extent that they read on the elected species. Claims 10, 14-24, 43 are withdrawn from consideration as being drawn to a non-elected invention. Claims 41-42 and 44-46 have been cancelled in favor of new claims 47-68.

Claim Rejections - 35 U5C § 112 first paragraph, Enablement

Claims 44-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Although the specification at paragraph [0040] of applicant's published application provides express basis for systemic administration:

> "[0040] In addition to topical administration, however, an in vivo application is also possible, in which the fibrinogen is systemically administered, for instance by means of an intravenous injection or infusion, or in any other method of administration suitable for the intended object."

claims 44-46 have been cancelled to further

prosecution and have been replaced by new claims limited variously to topical, intravenous or infusion modes of administration.

Claim Rejections – 35 U5C § 112 second paragraph, Indefinite

Claims 44-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Although the specification at paragraph [0040] of applicant's published application provides express basis for systemic administration:

> "[0040] In addition to topical administration, however, an in vivo application is also possible, in which the fibrinogen is systemically administered, for instance by means of an intravenous injection or infusion, or in any other method of administration suitable for the intended object."

claims 44-46 have been cancelled to further prosecution and have been replaced by new claims limited variously to topical, intravenous or infusion modes of administration.

Claim Rejections – 35 USC § 102

Claims 41, 42 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Hasegawa *et al.* or Holm *et al.*

Claims 41, 42 have been cancelled.

Claim Rejections – 35 USC § 103

Claims 44-46 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/62833 in combination with Holm *et al.* or Hasegawa *et al.*

Claims 44-46 have been cancelled.

New Claims

Applicant extends appreciation to the examiner for suggesting what may be claims of allowable scope. New claims 47-54 are believed to commensurate in scope to those the examiner suggested might be allowable. However, applicant further believes the scope suggested by the examiner is too narrowly drawn.

Applicant believes support also exists for intravenous or infusion modes of administration as set forth at paragraph [0040] of the published application:

> "[0040] In addition to topical administration, however, an in vivo application is also possible, in which the fibrinogen is systemically administered, for instance by means of an intravenous injection or infusion, or in any other method of administration suitable for the intended object."
>
> [0037] According to another preferred embodiment, the invention relates to a method in which the fibrin matrix is formed in vivo, the fibrinogen, optionally together with a suitable enzyme, such as thrombin, and optionally factor

> XIIIa and CaCl.sub.2, being applied in the place where the formation of a fibrin matrix takes place (topical administration). For instance, the fibrinogen is applied to inhibit or prevent tumor growth, cicatrization, adhesions and the like, or to promote the healing of burns and other wounds.

Holm et al. describe the purification and characterization of HMW, LMW, and LMW' resulting in a high purity of the different fibrinogens. Hasegawa et al. disclose the location of the binding site "b" for lateral polymerization of fibrin in the C-terminal half of HMW, which is missing in one of the two amino acid chains of LMW.

Neither Holm et al. nor Hasegawa et al. disclose a method for accelerating or decelerating angiogenesis by topically administering, intravenous injection and infusion, respectively, a fibrin matrix having a HMW content of at least 80 % (w/w) and a LMW content of at least 40 % (w/w), respectively. Therefore, none of these documents anticipates the subject matter of the newly presented claims.

WO 00/62833 A1 refers to a fibrin matrix comprising endothelial cells disposed on microcarrier particles, wherein the endothelial cells are, for example, introduced into a tissue to promote angiogenesis. WO 00/62833 A1 does not provide any information to a fibrin matrix comprising endothelial cells not disposed on microcarrier particles.

Moreover, WO 00/62833 A1 does not provide any hint to a fibrin matrix allowing decelerating angiogenesis either in

vitro or in vivo. Hence, WO 00/62833 A1 does not teach a fibrin matrix suitable for accelerating or decelerating angiogenesis depending on the HMW and LMW content, and does even not provide a hint to such effect.

Therefore, the skilled person is not motivated to combine WO 00/62833 A1 with Holm et al. referring to the three different fibrinogens HMW, LMW, and LMW', and even less to combine WO 00/62833 A1 with Hasegawa et al. describing the binding site "b" for lateral polymerization of fibrin.

Additionally, WO 00/62833 A1 does not guide the skilled person to a method wherein the fibrin matrix is administered topically, via intravenous injection or infusion to accelerate or decelerate angiogenesis depending on the disease to be treated.

As neither WO 00/62833 A1 alone nor a combination with Holm et al., or Hasegawa et al. renders the method of claims 47 or 51 obvious, allowing opposite effects depending on the HMW and LMW content, the subject matter of the new set of claims is inventive in view of WO 00/62833 A1, Holm et al., and Hasegawa et al., respectively.

at the examiner's suggestion, applicant is attaching the Declaration of Dr. Koolwijk in support of this application.

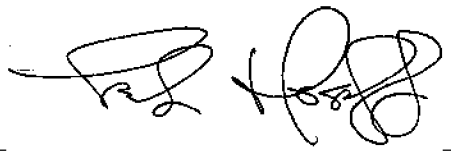
For all of the foregoing reasons, it is respectfully submitted that all of the claims now present in the application are clearly novel and patentable over the prior art of record, and are in proper form for allowance. Accordingly, favorable reconsideration and allowance is

respectfully requested. Should any unresolved issues remain, the Examiner is invited to call Applicants' attorney at the telephone number indicated below.

The Commissioner is hereby authorized to charge payment for any fees associated with this communication or credit any over payment to Deposit Account No. 14-1263.

Respectfully submitted,

NORRIS McLAUGHLIN & MARCUS, P.A.



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